Pericentric inversion of chromosome 7 (inv(7)(p22q11.2)) and ring chromosome 8 (r(8)(p23q24.3)) in a girl with minor anomalies

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Abstract

A 13 year old girl was referred with congenital microcephaly, developmental delay, a prominent nose, highly arched palate, and an apparently low set left ear. She was found to have a pericentric inversion of one chromosome 7 and a ring chromosome 8, 46,XX,inv(7)(pter→p22::q11.23→p22::q11.23→qter), r(8)(p23q24.3). The concurrence of these two abnormalities is a rare event and has not been reported previously.

To our knowledge there are only three reports in which pericentric inversion of chromosome 7 was noted as the sole abnormality.¹⁻³ The breakpoints involved in these reports were 7p13q22 and 7p12q11.23. We report on a new case of a pericentric inversion with breakpoints in 7p22q11.23 in a child who also had a ring chromosome 8, 46,XX,inv(7)(p22q11.23),r(8)(p23q24.3). Ring chromosome 8 is also a rare occurrence.^{4,5} Pericentric inversion of chromosome 7 coupled with a ring chromosome 8 is an unusual finding which has not been reported previously.

Case report

A 13 year old girl was referred for neurological evaluation because of developmental delay. She was known to have congenital microcephaly. She was delivered at 40 weeks of gestation to a 30 year old, gravida 2, para 1 mother. The mother reported decreased fetal movements during the pregnancy. The infant was born by spontaneous vaginal delivery with a birth weight of 2000 g and a head circumference of 29 cm. There were no postnatal complications.

Psychomotor development was delayed. She walked unaided at 2½ years, but at 13 years said no words, was not toilet trained, and was unable to feed herself. On physical examination, she was active and alert with self-stimulatory behaviour and no social contact. She did not talk and appeared to be profoundly cognitively impaired. Her weight was 30.4 kg and her head circumference was 46.5 cm., which is significantly below the 2nd centile. She had a prominent nose, a high arched palate, and an apparently low set left ear. Sexual development was Tanner stage 4. Her cardiovascular and respiratory systems were normal and the abdomen was normal on palpation. Her feet were held in plantar flexion with an equinovarus deformity.

She had normal cranial nerves and normal tone but there was limitation of dorsiflexion of the feet and joints, on the left more than the right. Strength was normal in all four limbs but she was hyperreflexic throughout, with bilateral flexor plantar responses. No cerebellar abnormalities were noted. The parents were cytogenetically normal; they refused photographic documentation.

Cytogenetic evaluation by G banding showed a pericentric inversion of chromosome 7 and ring chromosome 8, 46,XX,inv(7)(p22q11.23),r(8)(p23q24.3)(figure). The position of the centromeres was identified by the CBG technique.⁶ One hundred metaphases were counted.

Discussion

Presumably, two independent events occurred which resulted in pericentric inversion of chromosome 7 and a ring chromosome 8. The genetic material in our patient is apparently lost from the telomeres of chromosome 8 while, apart from the inversion, chromosome 7 remains apparently intact. Surprisingly, when 100 metaphases were analysed, neither acentric fragments nor double sized rings were observed.

Major clinical manifestations of two earlier reports of ring chromosome 8 as the sole abnormality included mental retardation, short stature and unusual facies,⁵ and multiple congenital anomalies.⁴ In addition, there are earlier case reports with a pericentric inversion also as the sole cytogenetic abnormality with the breakpoints at 7p13q22 and 7p12q11.23. The breakpoints in our case were at bands 7p22q11.23. In two previous cases,^{2,3} Zellweger syndrome was associated with a pericentric inversion of chromosome 7 band p12q11.23, while lethal osteogenesis imperfecta was suggested to be associated with 7p13q22 by Knisely *et al.*¹ Our patient with her 'double trouble' genetic defects presents neither of these clinical conditions. One can only speculate whether the minor anomalies noted in our case are the result of pericentric inversion of chromosome 7, or of ring chromosome 8, or both abnormalities. Owing to the complex nature of the aberrations involved, genetic counselling of the parents is difficult.

- 1 Knisely AS, Richardson A, Abuelo D, Casey S, Singer DB. Lethal osteogenesis imperfecta associated with 46,XY,inv(7)(p13q22) karyotype. *J Med Genet* 1988; 25:352-5.
- 2 Naritomi K, Hyakuna N, Suzuki Y, Orii T, Hirayama K. Zellweger syndrome and a microdeletion of the proximal long arm of chromosome 7. *Hum Genet* 1988;80:201-2.

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Karyotype of proband showing pericentric inversion of chromosome 7 and ring chromosome 8, 46,XX,inv(7)(p22q11.23),r(8)(p23q24.3). The centromeres were identified by CBG technique (inset).

- 3 Naritomi K, Izumikawa Y, Ohshiro S, *et al.* Gene assignment of Zellweger syndrome to 7q11.23: report of second case associated with a pericentric inversion of chromosome 7. *Hum Genet* 1989;84:79–80.
- 4 Hamers AJH, Van Kempen C. Ring chromosome 8 in a boy with multiple congenital abnormalities and mental retardation. *J Med Genet* 1977;14:451–5.

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